

WHAT IS CLAIMED IS:

1. A method of applying at least one agent selected from the group consisting of bioactive materials, flavorants, polymerization initiators, and polymerization rate modifiers to an applicator tip for an adhesive applicator, comprising:

dissolving or dispersing said agent in a low boiling point solvent to form a solution;

- applying said solution to said applicator tip; and  
drying said applicator tip;

wherein the low boiling point solvent comprises methanol.

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The method of claim 1, wherein the agent is dissolved in the low boiling point solvent.

3. The method of claim 1, wherein the agent is selected from the group consisting of polysorbate 20, polysorbate 80, poloxamers, tetrabutylammonium bromide, alkylbenzylalkonium chloride, stannous octoate (tin (II) 2-ethylhexanoate), sodium tetradecyl sulfate, and dodecyltrimethyl(3-sulfopropyl)ammonium hydroxide.

4. The method of claim 1, wherein the agent is selected from the group consisting of imidazole, tryptamine, urea, arginine, povidine, triphenylphosphine, triethyl phosphite, ethylene glycol, methyl gallate, ascorbic acid, tannins, tannic acid, sodium bisulfite, magnesium hydroxide, calcium sulfate, sodium silicate, thiourea, monensin, nonactin, crown ethers, calixarenes, polymeric epoxides, diethyl carbonate, di-t-butyl peroxide, and azobisisobutyronitrile.

5. The method of claim 1, wherein the agent is alkylbenzyltrimethylammonium chloride with an alkyl containing 6-18 carbon atoms, its pure components, or mixtures thereof.

6. The method of claim 1, wherein the agent comprises at least one member selected from the group consisting of antibiotics, antimicrobials, antiseptics, bacteriocins, bacteriostats, disinfectants, steroids, anesthetics, antifungal agents, anti-inflammatory agents, antiviral agents, antitumor agents, and antibacterials.

7. The method of claim 1, wherein the agent comprises crystal violet.

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8. The method of claim 7, wherein said crystal violet is present in an amount sufficient to provide effective antiviral, antimicrobial and/or antifungal properties to a polymerized adhesive composition.

5 9. The method of claim 7, wherein said crystal violet is present in an amount sufficient to initiate polymerization of a monomeric adhesive composition without providing effective antiviral, antimicrobial and/or antifungal properties to the adhesive composition subsequent to polymerization.

10 10. The method of claim 1, wherein the agent comprises a mixture of (i) at least one member selected from the group consisting of polymerization initiators and polymerization rate modifiers, and (ii) at least one member selected from the group consisting of bioactive materials and flavorants.

15 11. The method of claim 1, wherein the agent comprises at least one compound that is both (i) at least one member selected from the group consisting of polymerization initiators and polymerization rate modifiers and (ii) a bioactive material.

12. The method of claim 11, wherein the agent is selected from the group consisting of antibiotics, antimicrobials, antiseptics, bacteriocins, bacteriostats, disinfectants, steroids, anesthetics, antifungal agents, anti-inflammatory agents, and antibacterials.

20 13. The method of claim 1, wherein the agent comprises at least one flavorant.

1 14. The method of claim 13, wherein the flavorant is selected from the group consisting of 5-fold orange oil, anethole, banana distillate, benzaldehyde, clove oil, cold pressed valencia orange oil, cold pressed grapefruit oil, cold pressed lemon oil, cold pressed lime oil, cucumber distillate, honey distillate, menthol, alkyl  
25 salicylates, monosodium glutamate, spearmint, wintergreen, cinnamon, citrus, cherry, apple, peppermint, peppermint oil, peppermint spirit, vanillin, thymol, ethyl vanillin, and mixtures thereof.

ohj 15. The method of claim 1, wherein said solvent is methanol.

30 16. The method of claim 1, wherein said solvent further comprises a low boiling point ketone or alcohol other than methanol.

17. The method of claim 1, wherein said solvent further comprises acetone.

18. The method of claim 1, comprising applying said solution to a distal end of the applicator tip and forming a concentration gradient of said agent that decreases from said distal end of the applicator tip towards a center and a proximal end of the applicator tip.

5 19. The method of claim 1, wherein said solution is applied to said applicator tip by a process comprising:

combining said solution and said applicator tip in a vessel;

sealing said vessel;

10 applying one of a vacuum or pressure to said vessel to degas air trapped in said applicator tip; and  
releasing said vacuum or pressure.

20. The method of claim 1, comprising affixing said applicator tip to an applicator tube before or while applying said solution to said applicator tip.

15 \* 21. The method of claim 1, wherein said applicator tip comprises a porous polyurethane, polyolefin, polyester, or polyamide.

\* 22. The method of claim 1, wherein said applicator tip comprises porous polyethylene.

23. The method of claim 1, wherein said applicator tip comprises polyurethane foam.

20 24. The method of claim 21, wherein said applicator tip has an average pore size of about 1  $\mu\text{m}$  to about 500  $\mu\text{m}$ .

25. An applicator tip made by the method of claim 1.

25 ~~26. A method of making an applicator for adhesives, comprising:  
preparing a conduit for a fluid polymerizable adhesive composition  
operably connected to an applicator tip so that fluid flowing through said conduit also  
flows through said applicator tip,  
wherein a bioactive material or flavorant is included on or in said  
applicator tip.~~

30 27. The method of claim 26, wherein said bioactive material or flavorant is applied to a pre-formed applicator tip.

28. The method of claim 27, wherein said bioactive material or flavorant is applied to the pre-formed applicator tip as a solution of the bioactive material or flavorant in a solvent.

29. The method of claim 28, wherein the solvent is subsequently removed by evaporation after the solution is applied to the applicator tip.

30. The method of claim 26, wherein said bioactive material or flavorant is introduced into or onto the applicator tip during the process of manufacturing the applicator tip.

31. The method of claim 30, wherein the applicator tip is formed by molding a precursor material in a mold.

32. The method of claim 31, wherein the bioactive material or flavorant is mixed with the precursor material prior to molding, or is applied as a release agent to the mold.

33. The method of claim 26, wherein said applicator tip comprises a porous, absorbent, or adsorbent material.

34. The method of claim 26, wherein said applicator tip comprises a fiber or a foam. *honey-comb, woven pattern*

35. The method of claim 26, wherein said applicator tip has a shape selected from the group consisting of conical, cylindrical, chisel or polygonal.

36. The method of claim 26, comprising:  
dissolving or dispersing said bioactive material or flavorant in a solvent to form a solution;

applying said solution to said applicator tip; and  
drying said applicator tip.

37. The method of claim 36, comprising applying said solution to a distal end of the applicator tip and forming a concentration gradient of said bioactive material or flavorant that decreases from said distal end of the applicator tip towards a center and a proximal end of the applicator tip.

38. The method of claim 36, comprising placing said applicator tip on or in an applicator tube before or while applying said solution to said applicator tip.

39. The method of claim 36, comprising placing said applicator tip on or in an applicator tube after applying said solution to said applicator tip.

40. The method of claim 26, wherein the bioactive material is present and comprises at least one member selected from the group consisting of antibiotics, antimicrobials, antiseptics, bacteriocins, bacteriostats, disinfectants, steroids,

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 anesthetics, antifungal agents, anti-inflammatory agents, antiviral agents, antitumor agents, and antibacterials.

41. The method of claim 26, wherein the bioactive material is present and comprises crystal violet.

5 42. The method of claim 41, wherein said crystal violet is present in an amount sufficient to initiate polymerization of a monomeric adhesive composition.

43. The method of claim 26, wherein the bioactive material is present and comprises at least one compound that is both (i) at least one member selected from the group consisting of polymerization initiators and polymerization rate modifiers and  
 10 (ii) bioactive.

44. The method of claim 43, wherein said compound is selected from the group consisting of antibiotics, antimicrobials, antiseptics, bacteriocins, bacteriostats, disinfectants, steroids, anesthetics, antifungal agents, anti-inflammatory agents, antiviral agents, antitumor agents, and antibacterials.

15 45. The method of claim 26, wherein the flavorant is present and comprises at least one material selected from the group consisting of fruit oil, vegetable oil, esters, heterocyclic compounds, fruit extract and vegetable extract.

46. The method of claim 26, wherein the flavorant is present and comprises at least one material selected from the group consisting of 5-fold orange oil, anethole, banana distillate, benzaldehyde, clove oil, cold pressed valencia orange oil, cold pressed grapefruit oil, cold pressed lemon oil, cold pressed lime oil, cucumber distillate, honey distillate, menthol, alkyl salicylates, monosodium glutamate,  
 20 spearmint, wintergreen, cinnamon, citrus, cherry, apple, peppermint, peppermint oil, peppermint spirit, vanillin, thymol, and ethyl vanillin.

25 47. The method of claim 26, wherein the flavorant is present and comprises at least one sweetener selected from the group consisting of sugars and sugar substitutes.

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 48. The method of claim 26, wherein the flavorant is present in combination with a delivery substrate for the flavorant.

30 49. The method of claim 48, wherein the delivery substrate is selected from the group consisting of waxes, gels, polyethylene glycol, polysorbate, agar, povidone, sodium stearate, starch, powdered sugar, high fructose corn syrup, fructose,

glycerin, hydrogenated glucose syrup, sorbitol, mannitol, sucrose, cellulose acetate phthalate, dextrose, and polyvinyl alcohol.

50. A method of applying at least one agent selected from the group consisting of bioactive materials, flavorants, polymerization initiators, and polymerization rate modifiers to an applicator tip for an adhesive applicator, comprising:

dissolving, dispersing or suspending said agent in a liquid medium to form a suspension or solution;

combining said suspension or solution and said applicator tip in a vessel;

sealing said vessel;

applying one of a vacuum or pressure to said vessel to degas air trapped in said applicator tip;

releasing said vacuum or pressure; and

optionally drying said applicator tip.

51. The method of claim 50, further comprising forcing said applicator tip below a surface of said suspension or solution.

52. A method of making an applicator tip for an adhesive applicator, comprising:

loading at least one active member selected from the group consisting of bioactive materials, flavorants, polymerization initiators and polymerization rate modifiers on an applicator tip prior to or during manufacturing of a structural material or shape of the applicator tip.

53. The method of claim 52, wherein the applicator tip is formed of a reticulated material.

54. The method of claim 53, wherein the reticulated material is formed by combining a precursor of said structural material with a basic agent to form said structural material that acts as a polymerization initiator or rate modifier.

55. The method of claim 54, wherein the basic agent is selected from the group consisting of caustic soda, hydroxides of light metals, ammonium hydroxide, caustic alcohol, silver nitrate, and mixtures thereof.

56. The method of claim 52, wherein the applicator tip is formed by molding a precursor material in a mold.

57. The method of claim 56, wherein said active member is mixed with the precursor material prior to molding, or is applied as a release agent to the mold.

58. The method of claim 52, wherein the applicator tip shape is formed by blowing a precursor material in a mold to form a foam of said structural material.

59. The method of claim 58, wherein said active member is mixed with the precursor material prior to blowing.

60. The method of claim 58, wherein said active member is loaded into the foam during the blowing process.

61. The method of claim 58, wherein said active member is loaded onto the foam by applying said active member as a release agent to the mold.

62. A method of making an applicator for adhesives, comprising:

(a) making an applicator tip according to the method of claim 52;

(b) operably connecting said applicator tip to a conduit for a fluid polymerizable adhesive composition so that fluid flowing through said conduit also flows through said applicator tip, before, during or after step (a).

63. The method of claim 62, further comprising placing a fluid polymerizable adhesive composition in said conduit and out of contact with said applicator tip, before, during or after either of steps (a) or (b).

64. The method of claim 63, wherein said adhesive composition comprises adhesive 1,1-disubstituted ethylene monomers.

65. The method of claim 63, wherein said adhesive composition comprises adhesive  $\alpha$ -cyanoacrylate monomers.

66. The method of claim 65, wherein said  $\alpha$ -cyanoacrylate monomers are selected from the group consisting of butyl and octyl  $\alpha$ -cyanoacrylates.

67. An applicator for a polymerizable adhesive, comprising an applicator tip made by the method of claim 52, attached to an applicator body.

68. The applicator of claim 67, wherein said applicator body comprises a conduit for a fluid polymerizable adhesive composition, and said applicator tip is operably connected to said conduit so that fluid flowing through said conduit also flows through said applicator tip.

69. The applicator of claim 67, wherein said applicator body is free of a polymerizable adhesive reservoir.

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70. The applicator of claim 69, wherein said applicator tip comprises a fiber or a foam.

71. The applicator of claim 69, wherein said applicator body is a solid structure.

5 72. The applicator of claim 68, further comprising a container of polymerizable adhesive physically separated from said applicator tip within said applicator or within a package containing said applicator.

73. The applicator of claim 72, wherein said polymerizable adhesive comprises a 1,1-disubstituted ethylene monomer.

10 74. The applicator of claim 73, wherein said monomer is an  $\alpha$ -cyanoacrylate.

75. The applicator of claim 74, wherein said monomer is selected from the group consisting of butyl and octyl  $\alpha$ -cyanoacrylate.

15 76. An applicator for a polymerizable adhesive, comprising an applicator tip attached to an applicator body, and at least one bioactive material or flavorant on or in said applicator tip.

20 77. The applicator of claim 76, wherein said applicator body comprises a conduit for a fluid polymerizable adhesive material and said applicator tip is operably connected to said conduit so that fluid flowing through said conduit also flows through said applicator tip.

78. The applicator of claim 76, wherein said applicator body is free of a polymerizable adhesive reservoir.

79. The applicator of claim 78, wherein said applicator tip comprises a fiber or a foam.

25 80. The applicator of claim 78, wherein said applicator body is a solid structure.

81. The applicator of claim 77, wherein the bioactive material is present and is also at least one member selected from the group consisting of polymerization initiators and polymerization rate modifiers.

30 82. The applicator of claim 77, wherein the bioactive material is present and is selected from the group consisting of antibiotics, antimicrobials, antiseptics, bacteriocins, bacteriostats, disinfectants, steroids, anesthetics, antifungal agents, anti-

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inflammatory agents, antibacterials, antiviral agents, antitumor agents, and mixtures thereof.

83. The applicator of claim 77, wherein the bioactive material is present and is selected from the group consisting of acetic acid, aluminum acetate, bacitracin, bacitracin zinc, benzalkonium chloride, betadine, calcium chloroplatinate, certrimide, 5 chloramine T, chlorohexidine phosphanilate, chlorohexidine, chlorohexidine sulfate, chloropenidine, chloroplatinatic acid, ciprofloxacin, clindamycin, clioquinol, cysostaphin, gentamicin sulfate, hydrogen peroxide, iodinated polyvidone, iodine, iodophor, minocycline, mupirocin, neomycin, neomycin sulfate, nitrofurazone, 10 non-onynol 9, potassium permanganate, penicillin, polymyxin, polymyxin B, polymyxin, polymyxin B sulfate, polyvinylpyrrolidone iodine, povidone iodine, 8-hydroxyquinoline, quinolone thioureas, rifampin, rifamycin, silver acetate, silver benzoate, silver carbonate, silver chloride, silver citrate, silver iodide, silver nitrate, silver oxide, silver sulfadiazine, silver sulfate, sodium chloroplatinate, sodium 15 hypochlorite, sodium sulfadiazine, sphingolipids, tetracycline, zinc oxide, and zinc sulfadiazine.

84. The applicator of claim 77, wherein the bioactive material is present and comprises crystal violet.

85. The applicator of claim 84, wherein said crystal violet is present in an amount sufficient to initiate polymerization of a monomeric adhesive composition. 20

86. The applicator of claim 77, wherein the bioactive material is present and comprises a zinc compound.

87. The applicator of claim 86, wherein said zinc compound is selected from the group consisting of zinc salts of cyanoacrylic acid, zinc salts of cyanoacetic acid, zinc salts of dicyanoglutaric acid, zinc salts of rosin, zinc oxide, zinc salts of 25 polycyanoacrylic acid, zinc salts of polyacrylic acid, zinc bacitracin, zinc salicylate, zinc stearate, zinc citrate, zinc lactate, and mixtures thereof.

88. The applicator of claim 77, wherein the flavorant is present and comprises at least one material selected from the group consisting of fruit oil, 30 vegetable oil, esters, heterocyclic compounds, fruit extract and vegetable extract.

89. The applicator of claim 77, wherein the flavorant is present and comprises at least one material selected from the group consisting of 5-fold orange oil, anethole, banana distillate, benzaldehyde, clove oil, cold pressed valencia orange oil,

cold pressed grapefruit oil, cold pressed lemon oil, cold pressed lime oil, cucumber distillate, honey distillate, menthol, alkyl salicylates, monosodium glutamate, spearmint, wintergreen, cinnamon, citrus, cherry, apple, peppermint, peppermint oil, peppermint spirit, vanillin, thymol, and ethyl vanillin.

5           90.     The applicator of claim 77, wherein the flavorant is present and comprises at least one sweetener selected from the group consisting of sugars and sugar substitutes.

          91.     The applicator of claim 77, wherein the flavorant is present in combination with a delivery substrate for the flavorant.

10           92.     The applicator of claim 91, wherein the delivery substrate is selected from the group consisting of waxes, gels, polyethylene glycol, polysorbate, agar, povidone, sodium stearate, starch, powdered sugar, high fructose corn syrup, fructose, glycerin, hydrogenated glucose syrup, sorbitol, mannitol, sucrose, cellulose acetate phthalate, dextrose, and polyvinyl alcohol.

15           93.     The applicator of claim 77, further comprising a container of polymerizable adhesive physically separated from said applicator tip within said applicator or within a package containing said applicator.

          94.     The applicator of claim 93, wherein said polymerizable adhesive comprises a 1,1-disubstituted ethylene monomer.

20           95.     The applicator of claim 94, wherein said monomer is an  $\alpha$ -cyanoacrylate.

          96.     The applicator of claim 95, wherein said monomer is selected from the group consisting of butyl and octyl  $\alpha$ -cyanoacrylate.

25           97.     The applicator of claim 77, wherein said applicator tip comprises a material selected from the group consisting of plastics, foams, rubber, thermosets, films, fibers, and membranes.

          98.     The applicator of claim 97, wherein said material is a foam.

          99.     The applicator of claim 77, wherein said applicator tip comprises a porous, absorbent, or adsorbent material.

30           100.    The applicator of claim 99, wherein said material is selected from the group consisting of polyurethane, polyolefin, polyester, and polyamide.

          101.    The applicator of claim 77, wherein the tip is comprised of a reticulated material.

102. The applicator of claim 101, wherein the reticulated material comprises a basic agent that initiates polymerization of said adhesive material.

103. A method of making a medical adhesive composition comprising:  
dispensing a polymerizable adhesive composition with the applicator  
5 tip of claim 77,

wherein the polymerizable adhesive composition, upon entering the applicator tip, solubilizes or disperses and mixes with said bioactive material or flavorant, thus producing said medical adhesive composition.

104. The method of claim 103, wherein the medical adhesive composition  
10 comprises a 1,1-disubstituted ethylene monomer.

105. The method of claim 103, wherein the medical adhesive composition comprises an  $\alpha$ -cyanoacrylate.

106. The method of claim 105, wherein said  $\alpha$ -cyanoacrylate is selected from the group consisting of butyl and octyl  $\alpha$ -cyanoacrylate.

107. The method of claim 103, wherein the medical adhesive composition is  
15 dispensed directly from said applicator onto a patient.

108. The method of claim 107, wherein the patient is an animal.

109. The method of claim 103, wherein the dispensed medical adhesive joins tissues.

110. The method of claim 103, wherein the dispensed medical adhesive  
20 covers damaged tissue.

111. A method of making a medical adhesive composition comprising:  
dispensing a polymerizable adhesive composition through the applicator tip of claim 25,

25 wherein the polymerizable adhesive composition, upon passing through the applicator tip, solubilizes or disperses and mixes with said at least one agent, thus producing said medical adhesive composition.

112. The method of claim 111, wherein the medical adhesive composition comprises a 1,1-disubstituted ethylene monomer.

113. The method of claim 111, wherein the medical adhesive composition  
30 comprises an  $\alpha$ -cyanoacrylate.

114. The method of claim 113, wherein said  $\alpha$ -cyanoacrylate is selected from the group consisting of butyl and octyl  $\alpha$ -cyanoacrylate.

115. The method of claim 111, wherein the medical adhesive composition is dispensed directly from said applicator onto a patient.

116. The method of claim 115, wherein the patient is an animal.

117. The method of claim 111, wherein the medical adhesive composition comprises a bioactive material.

118. The method of claim 111, wherein the dispensed medical adhesive composition joins tissues.

119. The method of claim 112, wherein the dispensed medical adhesive composition covers damaged tissue.

120. An applicator for a polymerizable adhesive, comprising:  
a conduit for a fluid polymerizable adhesive material; and  
an applicator tip according to claim 25.

121. The applicator of claim 120, wherein the applicator is sterilized.

122. The applicator of claim 77, wherein the applicator is sterilized.

123. An applicator for a polymerizable adhesive comprising:  
a conduit for a fluid polymerizable adhesive material; and  
an applicator tip operably connected to said conduit so that fluid flowing through said conduit also flows through said applicator tip;

wherein said applicator tip has a gradient of a polymerization initiator or polymerization rate modifier disposed therein.

124. The applicator of claim 123, wherein the gradient shows a decrease in concentration of the initiator from a distal end of the applicator tip to a proximal end of the applicator tip.

125. A kit comprising a saleable package containing:  
a container that contains a polymerizable monomer composition, and  
an applicator according to claim 76.

126. The kit of claim 125, wherein said bioactive material or flavorant is a polymerization initiator or polymerization rate accelerator and causes polymerization of the polymerizable monomer composition to form a polymeric adhesive.

127. The kit of claim 125, wherein the polymerizable monomer is a 1,1-disubstituted ethylene monomer.

128. The kit of claim 127, wherein the polymerizable monomer is an  $\alpha$ -cyanoacrylate.

129. The kit of claim 128, wherein the  $\alpha$ -cyanoacrylate is selected from the group consisting of butyl and octyl  $\alpha$ -cyanoacrylate.

130. The kit of claim 125, wherein the bioactive material or flavorant is crystal violet.

5 131. The kit of claim 125, wherein the kit is sterilized.

132. The kit of claim 125, wherein the applicator is a swab attached to an applicator handle.

133. The kit of claim 125, wherein the container is operably connected for fluid flow from the container into the applicator.

10 134. The kit of claim 125, wherein the container is separate from the applicator.

135. An applicator for applying a polymerizable monomeric adhesive composition, comprising:

15 an applicator body, and  
an applicator tip attached to the applicator body,  
wherein said applicator body is free of a polymerizable adhesive reservoir, and

20 wherein at least one agent selected from the group consisting of bioactive materials, flavorants, polymerization initiators, and polymerization rate modifiers is present on or in said applicator tip.

136. The applicator of claim 135, wherein said applicator body is a solid structure.

25 137. The applicator of claim 135, wherein the agent comprises at least one member selected from the group consisting of antibiotics, antimicrobials, antiseptics, bacteriocins, bacteriostats, disinfectants, steroids, anesthetics, antifungal agents, anti-inflammatory agents, antiviral agents, antitumor agents, and antibacterials.

✓ 138. The applicator of claim 135, wherein the agent comprises crystal violet.

30 139. The applicator of claim 138, wherein said crystal violet is present in an amount sufficient to provide effective antiviral, antimicrobial and/or antifungal properties to a polymerized adhesive composition.

140. The applicator of claim 138, wherein said crystal violet is present in an amount sufficient to initiate polymerization of the polymerizable monomeric adhesive

composition without providing effective antiviral, antimicrobial and/or antifungal properties to the adhesive composition subsequent to polymerization.

141. The applicator of claim 135, wherein the agent comprises a mixture of (i) at least one member selected from the group consisting of polymerization initiators and polymerization rate modifiers, and (ii) at least one member selected from the group consisting of bioactive materials and flavorants.

142. The applicator of claim 135, wherein the agent comprises at least one compound that is both (i) at least one member selected from the group consisting of polymerization initiators and polymerization rate modifiers and (ii) a bioactive material.

143. The applicator of claim 135, wherein the applicator is a swab attached to an applicator handle.

144. A kit comprising a saleable package containing:  
a container that contains a polymerizable monomer composition, and  
an applicator according to claim 135.